

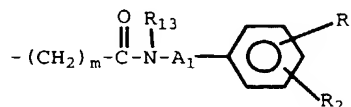
What is claimed is:

1. A diagnostic agent comprising an aminocarboxylate ligand complexed with a paramagnetic metal ion wherein a nitrogen atom within said
5 aminocarboxylate is substituted with a substituted aromatic amide group.

2. The diagnostic agent of claim 1 wherein said substituted aromatic amide group is of the formula

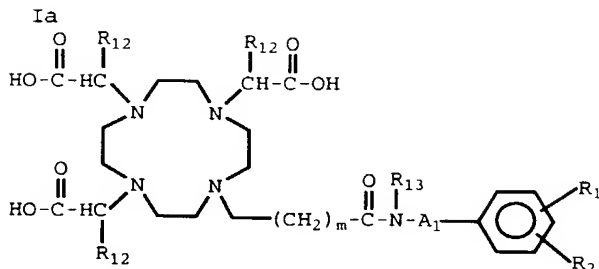
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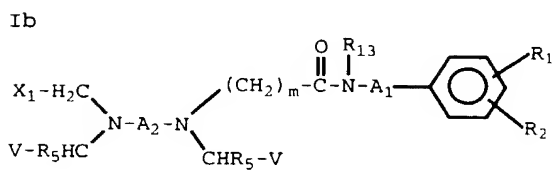


wherein

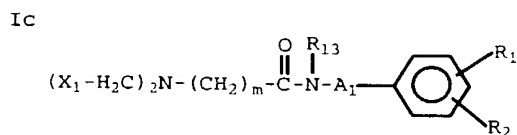
15 A_1 is $-(CH_2)_{m'}$ or a single bond;
 $(CH_2)_m$ and $(CH_2)_{m'}$ may independently be substituted with alkyl or hydroxyalkyl;
 R_1 and R_2 are each independently hydrogen, alkyl, $-NO_2$, $-NH_2$, $-\overset{\overset{S}{\parallel}}{N}HCNHR_{12}$, NCS , $-\overset{\overset{O}{\parallel}}{C}-NR_3R_4$, NR_3COR_9 where R_9 is alkyl or hydroxyalkyl, with the proviso
20 that at least one of R_1 and R_2 must be other than hydrogen;
 R_3 and R_4 are independently hydrogen, alkyl, arylalkyl, aryl, alkoxy and hydroxyalkyl;
 R_{12} is hydrogen, alkyl or hydroxyalkyl;
25 R_{13} is hydrogen, alkyl, arylalkyl, alkoxy or hydroxyalkyl;
 m and m' are independently 1 to 5;
and multimeric forms thereof.



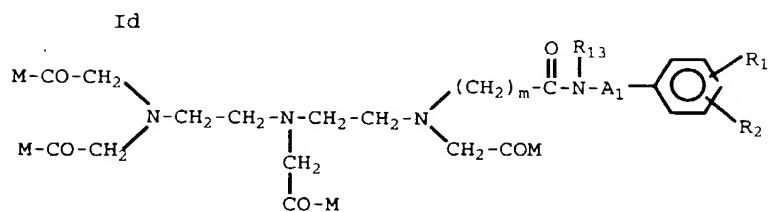
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wherein m , R_{13} , A_1 , R_1 , R_2 , and R_{12} are as defined in claim 2 and wherein

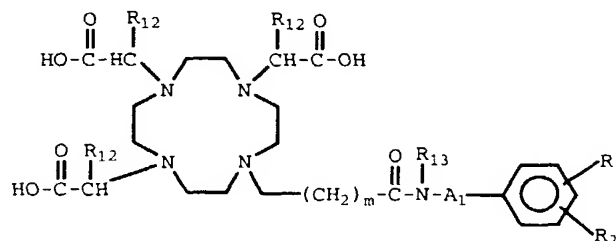
- X_1 is $-\text{COOY}_1$, PO_3HY_1 or $-\text{CONHOY}_1$;
 Y_1 is a hydrogen atom, a metal ion equivalent and/or a physiologically biocompatible cation of an inorganic or organic base or amino acid;
- 5 A_2 is $-\text{CHR}_6-\text{CHR}_7-$, $-\text{CH}_2\text{CH}_2(\text{ZCH}_2-\text{CH}_2)_n-$,
 $\text{N}(\text{CH}_2\text{X}_1)_2$ $\text{CH}_2-\text{CH}_2-\text{N}(\text{CH}_2\text{X}_1)_2$
 $-\text{CH}_2-\text{CH}-\text{CH}_2$ or $-\text{CH}_2-\text{CH}_2-\text{N}-\text{CH}_2-\text{CH}_2-$, wherein
 X_1 is as defined above;
each R_5 is hydrogen or methyl;
 R_6 and R_7 together represent a trimethylene
10 group or a tetramethylene group or individually are hydrogen atoms, lower alkyl groups (e.g., 1-8 carbons), phenyl groups, benzyl groups or R_6 is a hydrogen atom and R_7 is $-(\text{CH}_2)_p-\text{C}_6\text{H}_4-\text{W}$ -protein where p is 0 or 1, W is $-\text{NH}-$, $-\text{NHCOCH}_2-$ or $-\text{NHCS}-$, protein
15 represents a protein residue;
 n is 1, 2 or 3;
 Z is an oxygen atom or a sulfur atom or the group NCH_2X_1 or $\text{NCH}_2\text{CH}_2\text{OR}_8$ wherein X_1 is as defined above and R_8 is C_1 -alkyl;
- 20 V is X_1 or is $-\text{CH}_2\text{OH}$, $-\text{CONH}(\text{CH}_2)_r\text{X}_1$ or $-\text{COB}$, wherein X_1 is as defined above, B is a protein or lipid residue, r is an integer from 1 to 12, or if R_5 , R_6 and R_7 are each hydrogen; then both V 's together form the group
- 25
- $$-(\text{CH}_2)_w-\overset{\text{CH}_2\text{X}_1}{\underset{|}{\text{N}}}-\text{CH}_2-\text{CH}_2-\overset{\text{CH}_2\text{X}_1}{\underset{|}{\text{N}}}-(\text{CH}_2)_w-$$
- where X_1 is as above, w is 1, 2 or 3, provided that at least two of the substituents Y_1 represent metal
30 ion equivalents of an element with an atomic number of 21 to 29, 42, 44 or 57 to 83; from 1 to 4, advantageously 2 or 3, and preferably 2 M's are $-\text{OH}$ and the balance independently are $-\text{OR}_{10}$, $-\text{NH}_2$,

-NHR₁₀ and/or NR₁₀R₁₀' wherein R₁₀ and R₁₀' are selected from an organic alkyl radical of up to 18 carbon atoms which may be substituted.

4. The diagnostic agent of claim 1 wherein said paramagnetic metal ion is gadolinium.

5. A compound of formula Ia, Ib, Ic or Id as defined in claim 3, including multimers thereof.

6. A compound of the formula



wherein

A₁ is -(CH₂)_m'- or a single bond;

(CH₂)_m and (CH₂)_m' may independently be substituted with alkyl or hydroxyalkyl;

R₁ and R₂ are each independently hydrogen,

alkyl, -NO₂, -NH₂, -NHCNHR₁₂, NCS, -C(=O)-NR₃R₄ and NR₃COR₉ where R₉ is alkyl or hydroxyalkyl, with the proviso that at least one of R₁ and R₂ must be other than hydrogen;

R₃ and R₄ are independently hydrogen, alkyl, arylalkyl, aryl, alkoxy and hydroxyalkyl;

R₁₂ is hydrogen, alkyl or hydroxyalkyl;

R₁₃ is hydrogen, alkyl, arylalkyl, aryl, alkoxy or hydroxyalkyl;

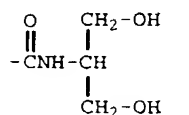
m and m' are independently 1 to 5; and multimeric forms thereof.

8. A compound of claim 6 wherein R_1 and R_2
 $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{NR}_3\text{R}_4 \\ | \\ -\text{CH}_2-\text{CH}-\text{CH}_2\text{OH} \\ | \\ \text{OH} \end{array}$
are each $-\text{CH}_2-\text{CH}-\text{CH}_2\text{OH}$ wherein each R_3 group is selected
from $-\text{CH}(\text{CH}_2\text{OH})_2$ and $-\text{CH}(\text{CH}_2\text{OH})_2$, and wherein each
 R_4 group is hydrogen.

9. A compound of claim 6 wherein R₁ and R₂

$$\text{are each } \begin{array}{c} \text{O} \quad \text{OH} \\ \parallel \quad | \\ \text{-CNHCH}_2\text{-CH-CH}_2\text{-OH} \end{array}$$

10 10. A compound of claim 6 wherein R₁ and R₂
are each



11 A compound of claim 6 having the name
15 10-[2-[[3,5-bis[(2,3-dihydroxypropyl)amino]-
carbonyl]phenyl]amino]-2-oxoethyl]-1,4,7,10-
tetraazacyclododecane-1,4,7-triacetic acid.

12. The gadolinium complex of the compound of claim 11.

20 13. A compound of claim 6 having the name
10-[2-[[3,5-bis-[[[2-hydroxy-1-(hydroxymethyl)-
ethyl]amino]carbonyl]phenylamino]2-oxoethyl]-
1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

14. The gadolinium complex of the compound of
25 claim 13.

15. A compound of claim 6 having the name
10-[2-[methyl[3,5-bis[[(2-methylbutyl)amino]-

carbonyl]phenyl]amino]-2-oxoethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

16. The gadolinium complex of the compound of claim 15.

5 17. A compound of claim 6 having the name 10-[2-[[4-[[2,3-dihydroxypropyl]amino]carbonyl]-phenyl]amino]-2-oxoethyl-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

10 18. The gadolinium complex of the compound of claim 17.

19. A compound of claim 6 having the name 10-[N-(4-nitrophenyl)acetamido]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

15 20. The gadolinium complex of the compound of claim 19.

21. A compound of claim 6 having the name 10-[N-(4-aminophenyl)acetamido]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

20 22. The gadolinium complex of the compound of claim 21.

23. A compound of claim 6 having the name 10-[[N-(4-(N'-isothiocyanato)phenyl)acetamido]]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

25 24. The gadolinium complex of the compound of claim 23.

25. A compound of claim 6 having the name 10-[N-[4-(N'-methylthioureido)phenyl]acetamido]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

30 26. The gadolinium complex of the compound of claim 25.

27. A compound of claim 6 having the name 10-[N-[4-(N',N'-diethylaminothioureido)phenyl]-acetamido]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

28. The gadolinium complex of the compound of claim 27.

29. A compound of claim 6 having the name
10,10'-[[[(1,2-ethanediyl)diimino]bis(thioxomethyl)-
5 diimino]bis(4,1-phenylene)]diimino-bis[1,4,7,10-
tetraazacyclododecane-1,4,7-triacetic acid].

30. The gadolinium complex of the compound of claim 29.

31. A compound of claim 6 having the name
10 10,10'-[[[(Thioxomethyl)bis(imino)bis(4,1-
phenylene)]bis(imino)]bis(2-oxo-2,1-ethanediyl)]-
1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

32. The gadolinium complex of the compound of claim 31.

15 33. A compound of claim 6 having the name
10,10',10''-[[[[[iminobis(2,1-ethanediyl)triimino]-
tris(thioxomethyl)]-triimino]tris-(4,1-phenylene)]-
triimino]tris(2-oxo-2,1-ethanediyl)]tris[1,4,7,10-
tetraazacyclododecane-1,4,7-triacetic acid].

20 34. The gadolinium complex of the compound of claim 33.

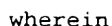
35. A compound of claim 6 having the name 10-
[2-[[2-(4-nitrophenyl)ethyl]amino]-2-oxoethyl]-
1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

25 36. The gadolinium complex of the compound of claim 35.

37. A compound of claim 6 having the name 10-
[2-[[3,5-bis[(2-hydroxyethyl)amino]-carbonyl]-
phenyl]amino]-2-oxoethyl]-1,4,7,10-tetra-
30 azacyclododecane-1,4,7-triacetic acid, monosodium salt.

38. The gadolinium complex of the compound of claim 37.

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$(CH_2)_m$ and $(CH_2)_{m'}$ may independently be

R_1 and R_2 are each independently hydrogen,

15 than hydrogen;

arylalkyl, aryl, alkoxy and hydroxyalkyl;

R₁₂ is hydrogen, alkyl or hydroxyalkyl;

20 alkoxy or hydroxyalkyl;

m and m' are independently 1 to 5;

and multimeric forms thereof.

40. A complex of claim 39 wherein R_1 and R_2

25 alkyl.

41. A complex of claim 39 wherein R_1 and R_2 are each $\begin{array}{c} \text{O} \\ || \\ -\text{C}-\text{NR}_3\text{R}_4 \\ | \\ \text{OH} \end{array}$ wherein each R_3 group is selected from $-\text{CH}_2-\text{CH}-\text{CH}_2-\text{OH}$ and $-\text{CH}(\text{CH}_2\text{OH})_2$, and wherein each R_4 group is hydrogen.

5 42. A complex of claim 39 wherein R₁ and R₂
 O OH
 || |
 are each -CNHCH₂-CH-CH₂-OH

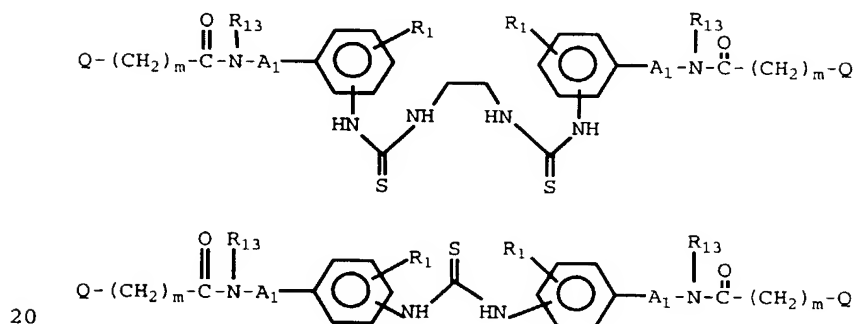
43. A complex of claim 39 wherein R_1 and R_2 are each

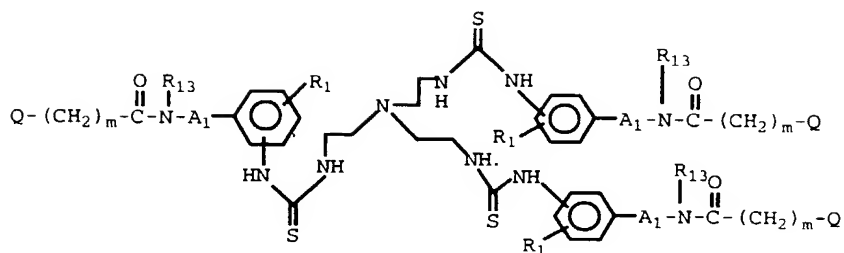


44. A complex of claim 39 wherein said metal atom is of atomic number 56-83.

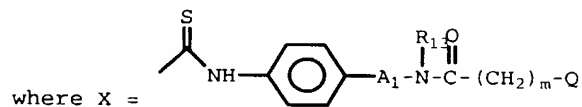
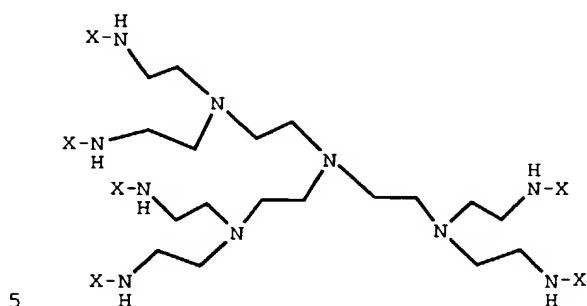
45. A complex of claim 39 wherein said metal
15 is gadolinium(III).

46. A multimer selected from





or



and wherein Q is an aminocarboxylate ligand and the
10 other variables are as defined in claim 3.

47. A compound of claim 6 having the name 10-[2-[[3,5-bis[[(2-methylbutyl)amino]carbonyl]-phenyl]amino]2-oxoethyl]1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid.

15 48. The gadolinium complex of the compound of
claim 47.

49. A compound of claim 6 having the name
10,10',10'',10''',10'''',10'''''-[[[[[[[[[[Nitrilo-

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50. The gadolinium complex of the compound of claim 49.